Quality Management System (QMS) for The Clinical Proteomic Tumor Analysis Consortium (CPTAC)

CPTAC Quality Manual

Table of Contents

List of Figures

List of Tables

Revision History

Rev	Date	Prepared By	Description of Change
000	2/1/2016	Battelle	First Draft
001	6/3/2016	Battelle	First release

1.0 Introduction

1.1 General

The Clinical Proteomic Tumor Analysis Consortium (CPTAC) program is a is a comprehensive and coordinated effort sponsored by the National Cancer Institute's (NCI) Office of Cancer Clinical Proteomics Research to accelerate the understanding of the molecular basis of cancer through the application of robust, quantitative, proteomic technologies and workflows. The National Cancer Institute (NCI) launched CPTAC as a technology assessment program in 2006. Phase II of the CPTAC program focused on providing proteomic analysis to selected biospecimens from The Cancer Genome Atlas (TCGA).

Now in its third phase, CPTAC is expanding the depth of analysis and breadth of tumor types to systematically explore the entire spectrum of proteomic and genomic changes involved in human cancer. The value of the data generated in CPTAC Phase III will lie in its quality, as all subsequent analyses and research outcomes will be dependent on the information generated.

To ensure the data completeness and the highest quality information, CPTAC focuses on quality as a best management practice. The CPTAC Quality Management System (QMS) serves as the basis by which the quality and value of the CPTAC data and information may be ensured.

1.2 CPTAC Path of Workflow

CPTAC's technical operations, known as the CPTAC Path of Workflow, is shown below.

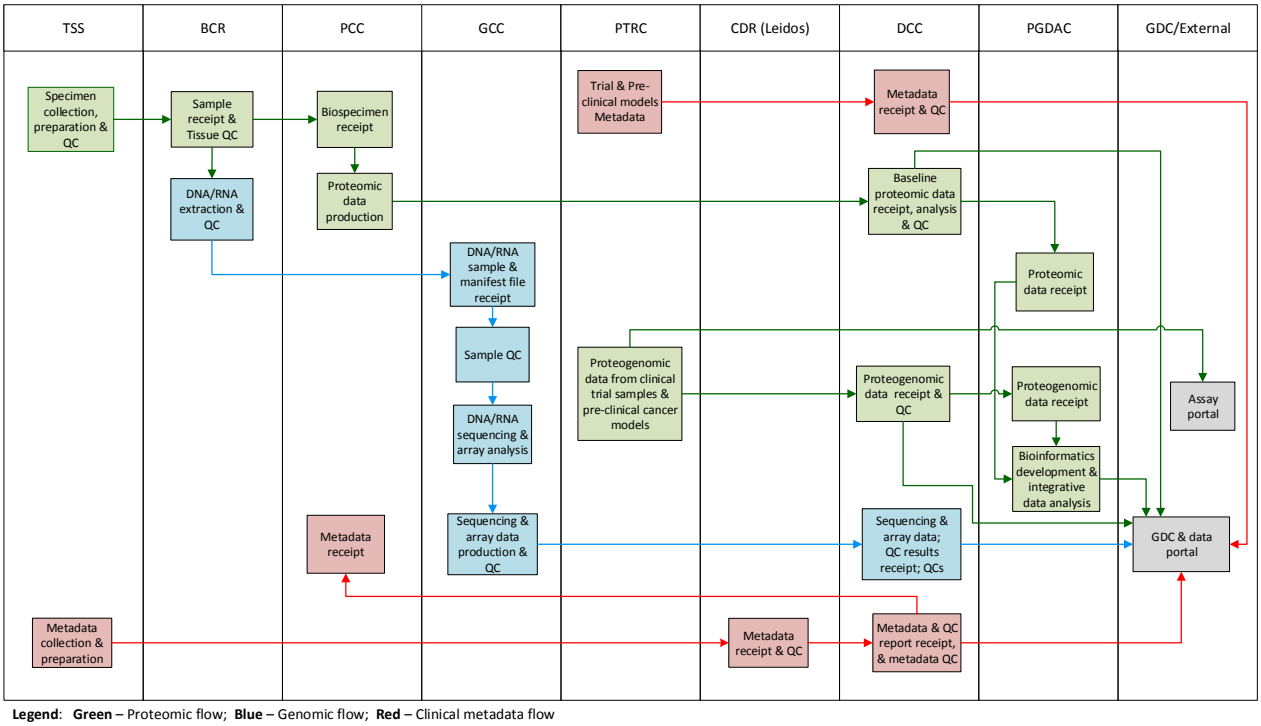

Figure 1. Detailed CPTAC Path of Workflow

Under specific agreements and conditions, Tissue Source Sites (TSSs) send clinical samples to the Biospecimen Core Resources (BCRs) and clinical data to the Comprehensive Data Resource (CDR). The BCRs receive and process the tissue samples; send proteins to the Proteome Characterization Center (PCC) and extracted DNA and RNA sample derivatives to the Genome Characterization Center (GCC) for analysis. The CDR sends clinical data to the Data Coordination Center (DCC). The PCC and GCC send sample analysis data to the DCC, which tracks data produced by these CPTAC components. The DCC also ensures that the data meet quality standards set for the project, and make CPTAC data publicly accessible through databases supported by NCI's Genome Data Commons (GDC). The DCC also establishes public and secure data resources that the Genome Data Analysis Center (GDAC) and worldwide scientists can use in their research to generate new insights into the causes and potential targets for interventions in cancer. Access to all CPTAC data is provided in a manner that meets the highest standards for protection and respect of the research participants. This information, which is rapidly deposited into public and secure databases for use by the research community, will accelerate efforts to find better ways of diagnosing, treating and, ultimately, cancer prevention.

1.3 CPTAC Vision, Mission and Values

Vision

- To accelerate the rate of scientific discovery and reduce the burden of cancer in the United States and around the world.

Mission

- To accelerate the understanding of the molecular basis of cancer through the application of robust, quantitative, proteomic technologies and workflows, and to use that understanding to identify biomarker candidates to enhance diagnosis, prevention and treatment of cancer.

Values

- Integrity and respect for:
    - **Our donors** and the confidentiality of their clinical data;
    - **The Cancer Research Community** to whom we provide timely, accurate, and reliable publically available data for research;
    - **Our Cancer Patients** to whom we hope to provide improved preventative, diagnostic, and therapeutic interventions;
    - **The U.S. society** that supports our biomedical research efforts through tax dollars
    - **Professionalism**; the expertise and competence of our CPTAC Staff and Awardees
    - **Ethics** and the demonstration of ethical and honest conduct
    - **Efficiency** and the best use of resources to provide accurate, reliable proteomic and genomic data more quickly and at a lower cost without compromising data quality
    - **Innovation** in techniques, analyses and applications to advance cancer research.

1.4 CPTAC Quality Management System

CPTAC's Quality Management System (QMS) will serve as the basis by which the quality and value of the CPTAC data is measured. It is the framework to manage and monitor all the activities of this complex

program, ensuring that the program achieves the quality necessary to accomplish the program goals. CPTAC management has established policies, processes, and procedures that define the expected quality of inputs and outputs needed by each component of CPTAC. QMS activities are designed to assure that each component within CPTAC has the quality materials, data, and information it needs including clinical data, tissue, genetic materials, proteomic and genetic data, and data analysis to meet or exceed the CPTAC program expectations.

CPTAC's QMS exists to provide the management and technical infrastructure needed to obtain, process, and characterize clinical data and biospecimen samples such that only the highest quality inputs of clinical data, sample materials, analytical data, and derived data are provided in the CPTAC database for research and public use.

The QMS provides guidance for the processes and procedures to organize for quality, provide for resources, and perform reviews of the status and effectiveness of CPTAC's quality management system.

1.5 CPTAC Quality Manual

The CPTAC Quality Manual (QM) exists to describe to CPTAC leadership, staff, and other components that form the CPTAC program how to manage our business with respect to providing the highest quality data and information. The QMS establishes our quality policies, processes, and procedures. This QM describes those policies, processes and procedures designed to meet these needs, and serves as "management's procedures manual" for management activities that support the CPTAC program.

When all CPTAC components work within an infrastructure of a QMS, the quality and integrity of our data and information is more likely to be assured. A simple graphic representation of the scope and structure of CPTAC's QMS is shown below.

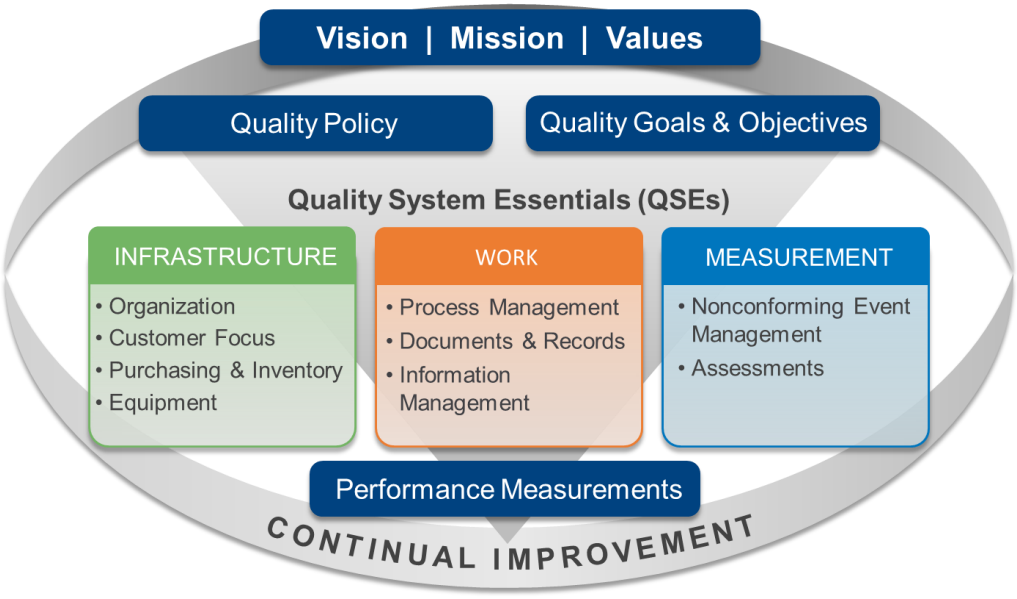

Figure 2. CPTAC QMS Model

1.6 The Quality System Essentials

The QMS provides guidance for CPTAC on the operational systems consisting of 12 Quality System Essentials (QSEs) that represent applicable regulatory, accreditation, and international requirements for managing the quality of proteomic and genomic data and information. The QSEs are inter-related and are incorporated throughout the CPTAC components:

- Organization
- Customer Focus
- Facilities and Safety (Note: This QSE is not included in the current QMS.)
- Personnel (Note: This QSE is not included in the current QMS embodiment.)
- Purchasing and Inventory
- Equipment
- Process Management
- Documents and Records
- Information Management
- Nonconforming Event Management
- Assessments
- Continual Improvement (Note: This QSE is not included in the current QMS embodiment.

1.7 Quality Manual Review and Update

The CPTAC's Quality Manual (QM) is reviewed at least annually by each CPTAC program component and is updated as needed; the Director of each CPTAC program component is responsible for ensuring annual review and approval or revision take place.

Because the overall CPTAC QM contains the collective policies, processes, and procedures for the entire QMS, changes are approved annually by the CPTAC Program Office to ensure that all components of the program are consistent within the QMS framework.

2.0 Organization

2.1. Quality Policy

CPTAC commits to using the latest state of the art technology to provide timely, accurate and reliable omic and other types of data in cancer biology and related technologies. Our quality management system supports this commitment, and guides the CPTAC research network in fulfilling our mission and meeting applicable requirements.

Please consider including the Quality Policy in all agreements with CPTAC components.

2.2 Quality Management System Maintenance

The CPTAC Program Office and components are committed to maintaining quality management systems to assure compliance with the requirements for good clinical data, biospecimen repository, proteomic and genomic analysis, informatics practice, and the organizational infrastructure for provision of accurate and reliable proteomic and genomic information.

2.3 Design for Organization Structure to Ensure Quality

2.3.1 CPTAC Program Office

- CPTAC's Contracting Officer's Representative is responsible for:
  - Ensuring strategic planning and research and development appropriate for CPTAC's needs
  - Active involvement in the design, implementation, and oversight of CPTAC's quality management system, and
  - Interaction with other components and staff as appropriate.
- Designated staff members are responsible for leadership and management of CPTAC and its quality management system.
- Designated quality managers and staff for their respective CPTAC component.

2.3.2 Ethics

The CPTAC Program Office and components do not involve themselves in activities that compromise our competence, impartiality, judgment, or operational integrity. We avoid internal and external commercial, financial, and other pressures and influences that may adversely affect the quality of our work. CPTAC activities will be consistent with the ethical guidelines of the institutions to which the CPTAC Program Office and components belong.

2.3.3 Organization Structure

CPTAC Program Office and component leadership and staff responsibilities, authorities, and interrelationships are defined and communicated. The CPTAC decision making organizational structure is outlined in Figure 3.

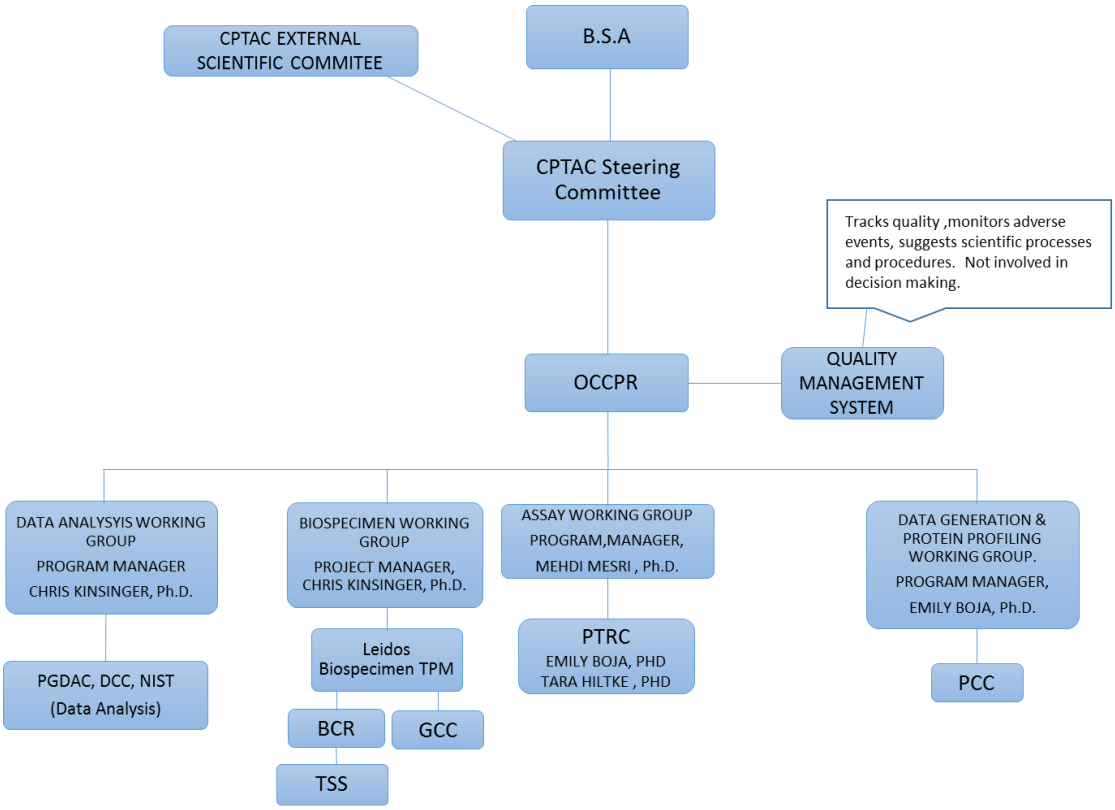

Figure 3. CPTAC Scientific Decision Making Organization Chart

2.3.4 Quality Managers

The CPTAC Program Office and components have appointed respective persons with defined responsibilities and authorities for oversight of the quality management system in their respective component's activities.

2.4 Effective Implementation of the QMS

2.4.1 Quality Manual

The CPTAC Quality Manual (QM) defines the structure and function of the QMS to staff and CPTAC's contractors and grantees, as well as defining the quality policy, goals and objectives.

2.4.2 Quality Policy

CPTAC's quality policy is understood and practiced by component leadership and staff as defined in 1.1.1 Quality Policy.

2.5 Allocation of Resources

CPTAC and its components shall identify and maintain resource requirements required for the facility, human, equipment, and materials needed for quality management and operational activities. Each component shall provide sufficient personnel with the appropriate skill mix to carry out the component's stated scope of work in order to achieve CPTAC's quality goals and objectives.

2.6 Planning for Quality

2.6.1 Quality Management System Planning

The CPTAC QMS applies to all CPTAC components and considers the needs and requirements of users. Planning of our quality management system is conducted annually through the Management Review Process (QMS.ORG.001) and is integrated with the overall business strategy so that we can meet the ongoing requirements of the system and quality objectives. We continually improve the effectiveness of our quality management system through the use of analytical and factual data on an ongoing basis.

2.6.2 CPTAC Quality Goals and Objectives

CPTAC has established quality goals and measurable quality objectives that are consistent with our quality policy and consider the needs and requirements of users.

The following are CPTAC quality goals:

- **Discovery Science** – to better understand the role of proteins, genes, and RNA in cancer biology
- **Translational Science** – to develop proteomic assays to aid clinical decision-making
- **Distribution of Research Resources** – data, antibodies, assays

Table 1 describes the CPTAC Quality Objectives for each of the established goals.

Table 1. CPTAC Phase III 2016 Quality Goals and Objectives

Goals	2016 CPTAC III Objectives
Discovery Science - To better understand the role of proteins, genes and RNA in cancer biology	• TSS: Collect 2,667 tumors within 2.5 years • BCR: Qualify 1,600 tumors within 3 years • PCC: Characterize 1,600 tumors within 5 years • GCC: Characterize 1,600 tumors within 4 years • DCC: Distribute data from 1,600 tumors within 5 years • CDR: Distribute clinical data from 1,600 tumors ▪ initial clinical data within 3 years ▪ distributing additional clinical data every year after • TCIA: Distribute medical images from 1,600 tumors within 3 years • PTRC: Analyze 500 cell lines within 5 years (animal models) • PTRC: Characterize 500 PDX within 5 years • PGDAC: Analyze, integrate, and/or visualize data from 1,600 tumors within 5 years • Consistent qualification/quality standards for processes for the duration of the CPTAC program for all components • Monitoring of time to process samples: • BCR: 20 samples to distribute to the PCC by Sept 2016 • BCR: Complete qualification of 1,600 biospecimens to PCC by Sept 2018 • GCC/DCC: All genomic data available by Sept 2019 • TSS: Baseline clinical data delivered 3 weeks after case qualified • BCR: Case qualified 3 months after receipt • Tracking current status of sample progress and sample invoices throughout the pipeline for all cases • Improve public interpretability of portal metrics; • Standardized metrics to legitimize proteomic analysis
Translational Science - To develop proteomic assays to aid clinical decision making	• Integrate clinical, genomic, and proteomic data; • Systematically identify proteins that derive from alterations in cancer genomes and related biological processes • Perform targeted protein measurement on preclinical cancer models to guide assay development for clinical trial samples • Applying fit for purpose proteomic assays to clinical trial samples addressing drug response and resistance mechanisms • Identification and addressing unmet clinical questions
Distributing Research Resources - data, antibodies, assays	• Provide Assay portal data with accompanying assays and protocols to the public • DCC: release characterization data to public, release genomic data to GDC • Provide antibody characterization data and accompanying antibodies to the antibody portal

2.6.3 Periodic Review of Quality Goals and Objectives

The CPTAC Program Office reviews the quality goals and objectives along with quality indicator results, with CPTAC components at a minimum on a quarterly basis to ensure relevancy and alignment with achieving its overall mission.

2.7 Management Review

2.7.1 Management Review Meeting

The CPTAC Program Office and component management review the QMS at planned intervals (minimally once per year) to determine its continuing suitability, adequacy, and effectiveness in accordance with QMS.ORG.001 Management Review Process. The Management Review includes assessing opportunities for improvement and changes needed to the QMS, including the Quality Policy, Goals and Objectives.

The output of the Management Review process is an input to future quality planning, change management and continual improvement of the QMS, for both planned and unplanned changes.

2.7.2 Quality Reports

The CPTAC Program Office and components prepare quality reports on a scheduled basis for management review (see QMS.ORG.001 Management Review Process). The quality reports contain but are not limited to, the following information:

- Findings from customer satisfaction feedback
- Summary information from CPTAC component quality control activities
- Summary information on CPTAC component nonconformances
- Data or summary information on CPTAC component performance on quality indicators
- Summary findings of CPTAC component internal audits
- Summary findings of CPTAC quality management system audits

See QMS.ORG.002 Quality Report Preparation.

2.8 Communication

The CPTAC Program Office has established processes to communicate to CPTAC components. CPTAC components have established processes to communicate to their respective staffs information to maintain and improve the effectiveness of CPTAC‘s QMS and to allow CPTAC Program Office and component staff to communicate concerns about program quality and safety to management. Staff are retrained and competency reassessed prior to implementation of a process change.

3.0 Customer Focus

3.1 Policy

The CPTAC Program Office and components are committed to providing the highest level of satisfaction by meeting or exceeding customer expectations, incorporating customer (user) needs, expectations, and requirements into the design of their respective services, seeking feedback from their internal and external customers, and improving services where needed.

3.1.1 Purpose

This policy provides direction for the processes and procedures needed to meet customer requirements so that CPTAC's end products are accurate and reliable.

3.1.2 Responsibility

- Identifying the expectations and requirements for all customer types, including external and internal.
- Determining the scope and process for seeking input and feedback from the component's users, and
- Incorporating such input and feedback into the component's work processes.

3.2 Identifying Customers and Their Expectations

The CPTAC Program Office and components identify the expectations of all customers of the CPTAC program, as well as incorporate those expectations into the design of processes in the CPTAC path of workflow. Customer requirements may vary by customer type or segment. External customers include CPTAC data or resource users not formally engaged in the CPTAC program. Internal customers are any component of the CPTAC Phase program and their staff members. See QMS.CF.001 Voice of the Customer Process.

3.3 Capability to Meet Customer Expectations

The CPTAC Program Office and components regularly assess their capabilities to meet customer expectations and design or improve their respective workflow processes to meet the needs, expectations, and requirements of their users. Any changes in the component's ability to continue meeting customer needs are immediately communicated to CPTAC program staff and affected customers, both external and internal.

3.4 Measuring Customer and User Satisfaction

3.4.1 External Customer Feedback

The CPTAC Program Office and components actively seek feedback, both positive and negative; from their external customers to determine whether their respective services meet their customers' needs, expectations, and requirements. Feedback and data are systematically analyzed to identify opportunities for improvement within the CPTAC path of workflow and the effectiveness of its QMS. Customer complaints are managed through the nonconforming event process. See QMS.NCE.001 Nonconforming Event Management Process.

3.4.2 Internal Customer Feedback

The CPTAC Program Office and components periodically gather feedback from staff and provide opportunities for staff to make suggestions for improvements to internal operations, and to identify additional opportunities for improvement that can affect their QMS or the component's ability to meet CPTAC's requirements.

3.5 Customer Complaints

The CPTAC Program Office and components manage customer complaints and ensure that all complaints are captured and reported immediately to the appropriate personnel for proper investigation and corrective action. Complaints are investigated, validated, their cause determined, and corrective action taken. Complaint data are aggregated to identify trends and opportunities for improvement that may impact CPTAC's ongoing ability to meet customer expectations. See QMS.NCE.001 Nonconforming Event Management Process.

4.0 Purchasing and Inventory

4.1 Policy

The CPTAC Program Office and components select and evaluate suppliers, purchase and receive materials and services as required for CPTAC. They also maintain respective inventory management processes.

4.1.1 Purpose

This policy provides direction for the processes and procedures to effectively acquire and manage CPTAC's purchased materials and services, and assures efficient and cost-effective operations for uninterrupted availability of biospecimen and related data.

4.1.2 Responsibility

The CPTAC Program Office is responsible for following NCI's established processes and procedures for selecting components, and for managing the inventory of CPTAC biospecimens.

CPTAC component management is responsible for establishing the component's purchasing, receiving, and inventory management processes.

CPTAC component staff is responsible for following established processes and procedures for requesting, receiving, and managing the component's materials and services.

4.2 Purchase of Materials or Services

The CPTAC Program Office and components identify their needed equipment, materials, and services as well as specify their respective requirements to suppliers.

The CPTAC Program Office and components qualify and select suppliers of their respective equipment, materials, and services based on the supplier's ability to meet their respective requirements.

CPTAC components maintain a current list of suppliers, contractors, and consultants that have been approved through their qualification process.

4.2.1 Purchase Agreements, Documents and Review

The CPTAC Program Office and components maintain formal purchase agreements with approved suppliers. The components prepare purchasing documents that contain specifications of the ordered equipment, materials, and services, in accordance with PM-0021, CPTAC Phase III Research Protocol, or other stated requirements. The components periodically review ongoing purchasing agreements and amend them as needed.

4.3 Supplier Evaluation

The CPTAC Program Office periodically evaluates the performance of selected components to ensure that CPTAC's expectations and the requirements of the QMS needed for program success are being fulfilled. These evaluations may be in addition to the annual Management Review.

CPTAC components periodically compare supplier performance to their respective specified expectations and requirements and follow up when necessary, including reporting their findings to the CPTAC Program

Office with contracting authority, and providing feedback to the supplier. See QMS.PUR.001 Supplier Performance Evaluation.

4.4 Receipt, Inspection, and Verification of Incoming Materials

CPTAC components maintain processes for receiving, inspecting, and verification (as needed) of incoming materials for acceptance before use to ensure all acceptance criteria and quality requirements have been met.

4.5 Storage and Handling of Materials

CPTAC components maintain designated storage areas for supplies and reagents to protect them from damage, deterioration or possible misuse in accordance with the manufacturer's recommendations and any applicable safety requirements.

4.6 Inventory Management

The CPTAC Program Office and components have documented processes to maintain respective inventory levels to ensure adequate supplies are on-hand to meet CPTAC requirements for sample and data collection. These processes also provide for proper conditions for storage and handling, and segregate uninspected and unacceptable materials from those accepted for use.

4.7 Traceability of Critical Materials and Services

CPTAC component work processes are designed to maintain traceability of critical materials and services that can affect the quality of results, and connect these to the appropriate samples, activities, and records. Chain of custody or other formal documents are maintained by the CPTAC Program Office and components and made accessible when needed.

5.0 Equipment

5.1 Policy

CPTAC components select, acquire, install, calibrate (where applicable), and maintain their respective equipment and instruments – including computer systems and software – and ensure these perform as expected for their intended use.

5.1.1 Purpose

This policy provides direction for the processes and procedures to effectively manage CPTAC components' equipment, instruments and computer systems.

5.1.2 Responsibility

CPTAC's component management is responsible for:

- The selection of equipment, instruments, and computer systems.

CPTAC component staff is responsible for:

- Performing assigned maintenance and calibrations, and using equipment according to manufacturer's instructions.

5.2 Selection, Qualification and Acquisition

CPTAC components maintain a process for identifying and selecting the component's equipment, instruments, and computer systems for their intended purpose. This process may include collaboration with other CPTAC components or functions where necessary.

5.2.1 Equipment Identification

CPTAC components assign each piece of equipment, instrument, or computer hardware a unique identification. Each CPTAC component maintains a current equipment list.

5.2.2 Equipment Qualifications

CPTAC components:

- Install equipment, instruments, and computer systems according to manufacturer's specifications (installation qualification)
- Verify that the functionality of equipment, instruments, and computer systems meets manufacturer's specifications (operational qualification)
- Verify that equipment, instruments, and computer systems perform as intended in their respective work processes, before actual use (performance qualification)
- Verify computer programs perform properly when first installed and on a scheduled basis, and
- Re-verify equipment, instruments, and computer system performance after any modifications.

5.2.3 Equipment Use and Maintenance

CPTAC components:

- Maintain schedules for periodic equipment, instrument, and computer software maintenance based on the manufacturer's recommendations
- Maintain procedures for daily maintenance according to manufacturer's instructions
- Perform the maintenance according to the schedules, or more frequently where needed, following the manufacturer's instructions
- Maintain a process for identifying, investigating, and following-up on malfunctioning equipment, instruments, and software including the impact of any effects on the quality of the final outputs, and verify that repaired or removed equipment, instruments, and any repaired or modified computer hardware or software meet required performance specifications before being returned to use.

5.2.4 Troubleshooting Service and Repair

CPTAC components track and maintain records of the following instrument, piece of equipment, and computer system service and repair:

- Troubleshooting and requalification before continued use
- Scheduled and unscheduled service performed by non-CPTAC staff
- Repairs performed by CPTAC staff and others.

5.2.5 Software Modifications

The CPTAC Program Office maintains a formal process for modifying a CPTAC Information Management System (IMS) software programs. See QMS.EQP.001 IMS Software Modifications Process.

5.3 Calibration

CPTAC components develop and follow formal calibration procedures for applicable instruments and equipment. These plans include:

- Schedules for calibration and calibration verification
- Responsibility for calibration
- Verification and recording of actions taken when verification of calibration fails to meet criteria
- Analysis of calibration results
- Posting of calibration status, due dates, and any needed adjustments or tolerances

5.4 Decommission and Final Disposition

CPTAC components formally decommission equipment no longer in use according to established protocols. Any confidential information is removed and stored in a secured location prior to removal from service. Any equipment exposed to biohazardous or toxic materials is decontaminated according to established component procedures before removal from the facility. A record of final disposition is maintained at each CPTAC component.

5.5 Equipment Records

As part of traceability, CPTAC components maintain records of each piece of equipment from acquisition through decommission, including at a minimum, the above-specified activities. These records should include:

- Name of equipment
- Model and serial number
- Location of equipment within the facility
- Date entered into service
- Qualification records that confirm suitability for use
- Calibration records
- Problem log
- Service and repair records
- Decommission and final disposition

6.0 Process Management

6.1 Policy

The CPTAC Program Office and components employ a process-based approach to managing the path of workflow to ensure the effectiveness and efficiency in meeting requirements and managing resources.

6.1.1 Purpose

This policy provides direction for the defined conditions to effectively ensure the quality of CPTAC component inputs, workflows, and outputs, so that the accuracy and integrity of CPTAC data and information can be assured.

6.1.2 Responsibility

The CPTAC Program Office is responsible for:

- Establishing processes and procedures and communicating the necessary requirements for process control and change management to CPTAC components
- Documenting and communicating the overall workflow for the CPTAC program.

CPTAC's component management is responsible for:

- Establishing standardized processes and procedures to manage their respective component's activities in the path of workflow, as well as controlling changes to any process or procedure within the path of workflow
- Ensuring that their respective component's workflows are accurately documented, validated, and communicated to staff

CPTAC and component staff members are responsible for:

- Following approved workflow processes and procedures without deviations
- Reporting any problems encountered in their work

6.2 Analysis, Design, and Documentation of Work Activities

6.2.1 Work Process Design and Analysis

The CPTAC Program Office and components incorporate customer, user, and quality requirements into the development of new or changed workflow processes and services, and the output of those processes are analyzed to determine if customer expectations are being met.

The CPTAC Program Office and components evaluate the impact of potential and actual work process failures on customers and users and take action to reduce or eliminate identified risks. See QMS.NCE.001 Nonconforming Event Management.

6.2.2 Process Documentation

The CPTAC Program Office and components maintain standardized, documented processes and procedures for the entire workflow to ensure consistency in performance and results. These may be in the form suitable for the component's needs, such as process maps or flowcharts, written instructions or other visual media. The CPTAC Program Office and components communicate workflow processes to staff

involved in executing the processes and procedures. New staff are trained and determined to be competent in their respective work processes and procedures before performing unsupervised work.

6.3 Process Validation and Verification

CPTAC components validate or verify—before implementation—that new or changed processes in their path of workflow perform as intended and meet customer and user expectations and requirements. All validations and verifications are documented and results recorded. The CPTAC Program Office and components control the implementation of new or changed processes (see QMS.PRM.001 Change Management Process).

6.3.1 Post-implementation Evaluation

The CPTAC Program Office and components evaluate the effectiveness of new or changed processes and procedures after implementation.

6.3.2 Comparability of Results

CPTAC components that perform technical methods using different procedures or equipment, or at different sites, or all of these, use a defined process at specified intervals to compare the procedures, equipment and methods used and verify the comparability of results.

6.4 Process Control

6.4.1 Process Performance

CPTAC component staff members follow approved workflow processes and procedures as implemented, without deviation. Planned deviations from established processes are justified and approved prior to being performed. Processes in the path of workflow (see section 0.2, Figure 1) are monitored to ensure maximum efficiency and effectiveness.

6.4.2 Quality Control

Monitoring and controlling processes require proper recording, review and evaluation of results. The CPTAC Program Office and components maintain quality control (QC) plans for their respective workflow processes to detect errors, and monitor the performance of the processes. QC plans should be designed to:

- Verify the intended quality of results and evaluate them against predefined acceptance criteria
- Investigate quality control failures before release of sample derivatives, data, and information
- Take action to prevent the release of any incorrect sample materials or results

Any discovered deviation is recorded as a nonconforming event in the IMS. See QMS.NCE.001 Nonconforming Event Management.

6.5 Change Management

The CPTAC Program Office and components maintain processes to ensure any change made to a controlled process in the CPTAC path of workflow is properly identified, validated and approved prior to implementation. Any change or modification to processes in the path of workflow must be approved by the CPTAC Program Office prior to implementation. See QMS.PRM.001 Change Management Process.

All related documents, including written instructions, flowcharts (workflows) and associated forms are updated to reflect the change.

Staff are retrained and competency reassessed prior to implementation of a process change.

7.0 Documents and Records

7.1 Policy

The CPTAC Program Office and components control their documents so that CPTAC component staff has access to only the most current versions through Huddle (https://ncicptac.huddle.net/workspace/37019494/files/#/folder/40540062/list). The CPTAC Program Office and components also control their records so that they are reviewed, archived, and stored in accordance with established record retention schedules.

7.1.1 Purpose

This policy provides direction for the processes and procedures to develop, manage, retain, and access accurate and complete CPTAC documents and records during the entire use and retention periods.

7.1.2 Responsibility

CPTAC's Program Office and components are responsible for:

- Establishing and maintaining document control processes and the records control processes.

CPTAC component management is responsible for:

- Implementing document control and record control in their respective facilities.

CPTAC component staff is responsible for:

- Using only the most current version of an approved document.

All CPTAC staff are responsible for:

- Maintaining the confidentiality and integrity of CPTAC records.

7.2 Document Management

7.2.1 Document Identification and Control

All CPTAC components, including the CPTAC Program Office, maintain a system for managing all documentation used for the CPTAC program to ensure their appropriate identification, approval, and availability for use. The CPTAC Program Office and components have systems in place for the identification, creation, review, and approval of their respective policies, processes, procedures, forms, and label documents in approved formats.

7.2.2 New Document Creation, Review and Approval

The CPTAC Program Office and components follow a systematic approach for the creation of documents on appropriate media to help manage their policies, processes, procedures, forms and labeling. External documents used in lieu of internal documents (e.g., equipment manufacturers' operator manuals, package inserts, etc.) are subject to the CPTAC component's document control system. Authorized CPTAC component staff review and approve each new or revised document before use. The CPTAC Program Office maintains a document master list in the QMS IMS of all the CPTAC components' processes and procedures.

7.2.3 Document Changes and Periodic Review

The CPTAC Program Office and components maintain processes for making changes to and approving revised documents to ensure only authorized changes are made, and that component staff are using the most current version. All changes are reviewed and approved before use. All documents that are included as part of the CPTAC program are periodically reviewed for correctness, completeness, and currency.

7.2.4 Archival, Storage, and Retention of Documents

The CPTAC Program Office and components promptly remove invalid and obsolete documents from all points of use and protect them from inadvertent use. Invalid and obsolete documents are archived or destroyed as appropriate, and stored in a manner that prevents accidental or unauthorized access, deterioration, damage, destruction, modification, or loss. CPTAC documents are retrievable during their established retention periods. See QMS.DOC.001 Control of Documents and Data.

7.3 Records Management

7.3.1 Records Control

The CPTAC Program Office and components maintain processes for the identification, collection, indexing, access, storage, maintenance, and safe disposal of its records. See QMS.DOC.002 Control of Records.

7.3.2 Creation of Records

Records created when entering data or information either electronically or in hard copy, are created in a manner which ensures legibility and completeness. Records are created at the time and place work is being performed. A master list of records is maintained by the CPTAC Program Office and each component to ensure that required records are generated.

7.3.3 Review of Records

The CPTAC Program Office and components maintain processes for periodic review of records of quality and technical activities, documenting the reviews, and taking appropriate follow-up action when needed. The frequency of reviews are in accordance with the individual component's policies and procedures or as needed for internal assessment purposes. Records are made available for review by the CPTAC Program Office as requested.

7.3.4 Changes to Records

The CPTAC Program Office and components maintain processes for making changes to electronic and paper records such that an audit trail is created and original information is not obscured. Original record information is retained.

7.3.5 Records Storage and Maintenance

The CPTAC Program Office and components store their respective documents and records in an organized manner that preserves legibility for the entire retention period; protects from accidental or unauthorized access, modification, deterioration, or destruction; and allows for access and retrieval within a time frame appropriate to the circumstances.

7.3.6 Access to Records

Archived records are maintained in a manner that ensures their accessibility throughout their retention period. Storage media that becomes obsolete requires those records to be transferred to a more suitable storage media while maintaining their legibility.

7.3.7 Retention of Records

The CPTAC Program Office and components retain respective archived records for time periods defined in their respective records retention schedule including any national, regional, or local requirements. Records pertaining to the CPTAC III QMS are maintained according to the CPTAC Records Retention Schedule.

7.3.8 Disposal of Records

The CPTAC Program Office and components dispose of records after their respective retention periods in a manner that ensures confidentiality of the information contained. A master list of all record destruction is maintained by each component.

8.0 Information Management

8.1 Policy

The CPTAC Program Office and components archive, maintain, transmit, and release data and information in their information systems in a manner that ensures integrity, controls access, and protects the confidentiality of protected health and other information.

8.1.1 Purpose

This policy provides direction for the processes and procedures to use, manage, and protect the data and information contained in CPTAC's written and electronic information systems. The CPTAC Information Management System (IMS) aids in the implementation and on-going management of the CPTAC Quality Management System (QMS).

8.1.2 Responsibility

All CPTAC Program Office and component staff are responsible for maintaining and managing data, protecting confidential information, and accessing only information authorized for their respective positions.

8.2 Planning for Information Needs

The CPTAC Program Office and components have defined the flow of data and information derived from the components' work processes and use this flow to assess current information needs and plan for future needs.

8.3 Confidentiality of Protected Information

The CPTAC Program Office and components maintain processes for receiving information from external sources and for releasing information to external sources in a manner that provides for the confidentiality of any protected information.

8.4 Access to Data and Information

The CPTAC Program Office and component management have assigned computer system access that are appropriate for each staff member's job functions. The CPTAC Program Office and components control access and maintain processes to prevent unauthorized access to, and release of, data and information. CPTAC components maintain a listing of all staff signatures, initials, user codes, and employment dates for persons who perform any part of the component's path of workflow or management thereof.

8.5 Data Integrity

CPTAC paper-based and electronic information systems maintain the integrity of data and information to ensure their retrievability and usability. CPTAC Program Office and component processes accurately and reliably transfer and transmit data and information from the point of entry to final destination in a timely manner. The CPTAC Program Office and components annually verify the accuracy of any new or changes to computer-driven calculations performed on data.

8.6 Availability During Downtime

8.6.1 Storage and Retrieval

The CPTAC Program Office and components store data and archived information so they are easily and readily retrievable within an established timeframe that is consistent with CPTAC component and user needs. All data storage media are labeled, stored, and protected from damage, unauthorized use, or unintended destruction. CPTAC Program Office and component processes ensure retrievability of data and information for the entire retention period.

8.6.2 Backup System

The CPTAC Program Office and components have defined processes for backup of all critical data and information. The backup system is periodically tested to ensure that data and information are restorable and usable. Backed-up data and information are protected from unauthorized access, loss, or modification.

8.6.3 Contingency Plans

The CPTAC Program Office and components have developed written contingency plans to handle services in the event of a computer or other information system failure, that provide for continued access to critical information in the event that computerized data or the primary source(s) of information are unavailable. The CPTAC Program Office and components periodically test their contingency plan to ensure its ongoing effectiveness.

9.0 Nonconforming Event Management

9.1 Policy

The CPTAC Program Office and components maintain the means to capture, investigate, analyze, and follow-up on events or outcomes that do not conform to CPTAC components' established policies, processes, and procedures, or that may interfere with expected customer or user requirements. These are referred to as nonconforming events (NCEs).

9.1.1 Purpose

This policy provides direction for the processes and procedures to document, investigate, track, analyze, and take corrective action on nonconforming events, complaints, and any other adverse events in the CPTAC path of workflow.

9.1.2 Responsibility

The CPTAC Program Office is responsible for:

- Monitoring and reviewing any nonconforming events reported in the CPTAC IMS with the respective CPTAC component
- Providing input to the components during the investigation of NCE's
- Reviewing and/or approving recommended changes impacting the CPTAC Phase III Research Protocol or CPTAC QMS.

CPTAC component staff is responsible for:

- Identifying and reporting any nonconforming events and complaints encountered in their work.

CPTAC component management staff is responsible for:

- Ensuring the appropriate remedial action is taken, as well as appropriate follow-up actions.

9.2 Identification of Nonconforming Events

9.2.1 Detection of Nonconforming Events and Complaints

CPTAC component staff members detect deviations or unexpected outcomes from their established policies, processes, and procedures through sources such as complaints, records, unexpected work events, reviews, adverse events, accidents, near misses, and during regular monitoring of performance data and assessment activities. Nonconforming events are entered into the CPTAC IMS so that they can be tracked and analyzed.

9.2.2 Immediate Action

Upon discovery of a deviation or nonconforming event, CPTAC component staff members take, and record in the CPTAC IMS, immediate (remedial) action to protect the quality of data and information and to prevent unintended distribution of any nonconforming sample material, data and information. CPTAC component management considers the significance of any nonconforming sample material, data, and information and informs other CPTAC components as needed.

9.2.3 Equipment Incident Reporting

CPTAC components record in the CPTAC IMS and investigate any adverse incidents or accidents attributed directly to specific equipment and report these to the manufacturer and to appropriate authorities, where required. A supplier corrective action plan may be requested as needed.

9.2.4 Product and Service Recalls

CPTAC components maintain processes for managing recalls of materials, equipment, or software and reports these to appropriate parties as required. In the event that recalled materials, equipment or software lead to a potential adverse event in the CPTAC path of workflow due to their use, the respective component is responsible for reporting the potential risk to the other appropriate components. These issues are recorded as nonconforming events in the CPTAC IMS.

9.3 Investigation of Nonconforming Events

The CPTAC Program Office and components maintain processes and procedures to investigate their respective nonconforming events and complaints and determine the scope of any adverse effects on the quality and integrity of its outputs. Results of investigations are entered into the CPTAC IMS.

9.3.1 Event Report

Records of each nonconforming event and complaint are maintained in the CPTAC IMS. These records are reviewed by designated CPTAC component personnel.

9.3.2 Corrective Action

When a nonconforming event is detected, CPTAC components take corrective action to document and eliminate the initial cause of the issue.

9.4 Classification, Analysis and Trending of Data and Information

The CPTAC Program Office and components monitor and review data and information from nonconforming event reports and complaints at regular intervals to detect trends and initiate actions to eliminate root causes and potential risks.

9.4.1 Root Cause Analysis

The CPTAC Program Office and components take a systematic, fact-based approach to identifying and eliminating the underlying causes of recurring or unwanted nonconforming events. Data and trend analyses provide critical input to this process and are used to objectively identify, investigate and develop potential solutions to detected problems. See QMS.NCE.002 Root Cause Analysis Process.

9.5 Management Review of Nonconforming Events

The CPTAC Program Office maintains a process for the components to report nonconforming event information to CPTAC management. See Organization Policy Section 1.7.2 Quality Reports.

10.0 Assessments

10.1 Policy

The CPTAC Program Office and components conduct internal assessments of their work processes and the QSEs to determine the effectiveness of the CPTAC Phase III Quality Management System.

10.1.1 Purpose

This policy provides guidance for the processes and procedures to manage and conduct internal assessments.

10.1.2 Responsibility

The CPTAC Program Office and components are responsible for coordinating and performing internal assessments with designated staff who are trained in this assessment process, and preparing for external assessments as required.

10.2 Internal Assessments

The CPTAC Program Office maintains a process to conduct scheduled internal assessments of the managerial and technical work processes of CPTAC components to ensure the QMS continually meets program requirements. Additionally, CPTAC components establish processes for managing internal assessments.

10.2.1 Internal Assessment Program

The CPTAC Program Office and components have established programs to conduct internal assessments of the QSEs and path of workflow in order to determine the effectiveness of the QMS and to ensure compliance to the requirements as specified by the CPTAC QMS.

10.2.2. Internal Assessors

Assessments are conducted by component staff or designated representatives who have received appropriate training in the assessment process. Internal assessors never assess any activity or area for which they have direct responsibility or function.

10.2.3 Internal Assessment Information

CPTAC components provide data, summary information, and findings from internal assessment activities for the preparation of a quality report (see Section 1.7 Management Review).

10.2.4 Quality Indicators

The CPTAC Program Office and components identify, implement, measure, and report quality indicators that are linked to the CPTAC Phase III quality goals and objectives to systematically monitor process performance across their entire respective paths of workflow. Quality indicators comprise a regular assessment of the implementation of the QMS.

10.3 External Assessments

CPTAC components should maintain a process to prepare for external assessment events, such as those conducted by governmental and accreditation organizations, if certifications are required by CPTAC. CPTAC components are also encouraged to participate in national or regional accreditation programs.

11.0 Key References

1. The Clinical Proteomic Tumor Analysis Consortium (CPTAC) Program: http://proteomics.cancer.gov/programs/cptacnetwork

2. CPTAC Data Portal: https://cptac-data-portal.georgetown.edu/

3. CPTAC Assay Portal: https://assays.cancer.gov

4. CPTAC Antibody Portal: https://antibodies.cancer.gov/

5. Clinical and Laboratory Standards Institute documents:

   - Quality Management System: A Model for Laboratory Services; Approved Guideline-Fourth Edition (QMS01-A4) 2011
   - QMS: Development and Management of Laboratory Documents; Approved Guideline-Sixth Edition (GP02-A6) 2013
   - Development and Use of Quality Indicators for Process Improvement and Monitoring of Laboratory Quality; Approved Guideline-First Edition (QMS12-A) 2010
   - The Key to Quality **(**K2Q**)** 2007
   - QMS: Equipment; Approved Guideline-First Edition (QMS13-A) 2011

6. ISO 9001:2015. Quality management systems – Requirements*.* Geneva, Switzerland: International Organization for Standardization; 2015

7. ISO 15189:2012. Medical Laboratories-requirements for quality and competence. Geneva, Switzerland: International Organization for Standardization; 2012

8. 21 CFR. Part 58, Good Laboratory Practice for Nonclinical Studies Reference. U.S. Government Printing Office via GPO Access, April 2015

12.0 Glossary

Assessment – process of gathering information on the condition of a process or activity.

Audit – systematic, independent and documented process for obtaining audit evidence (ISO 9000 [3.9.4]) and evaluating it objectively to determine the extent to which audit criteria are fulfilled (ISO 9000 [3.9.1]).

Competence – demonstrated personal attributes and demonstrated ability to apply knowledge and skills (ISO 9000 [3.1.6]).

Continual improvement (CI) – includes the actions taken throughout an organization to increase the effectiveness and efficiency of activities and processes in order to provide added benefits to the customer and organization. (Westcott, Russell T., *The Certified Manager of Quality / Organizational Excellence Handbook,* 3rd ed., American Society of Quality Press, 2006.)

Corrective action – action to eliminate the cause of a detected nonconformity or other undesirable situation (ISO 9000 [3.6.5]); **NOTE 1:** There can be more than one cause for a nonconformity; **NOTE 2:** Corrective action is taken to prevent recurrence whereas preventive action (ISO 9000 [3.6.4]) is taken to prevent occurrence.

Customer – organization or person that receives a product (3.3.5) (ISO 9000); EXAMPLES: Consumer, client, end user, retailer, beneficiary, and purchaser; **NOTE 1:** A customer can be internal or external to the organization; **NOTE 2:** Employees may be regarded as internal customers.

Document – information and its supporting medium (ISO 9000 [3.7.2]); **NOTE:** This may be paper-based or electronic.

Effectiveness – extent to which planned activities are realized and planned results achieved (ISO 9000 [3.2.14]).

Efficiency – relationship between the results achieved and the resources used (ISO 9000 [3.2.15]).

Error – a deviation from truth, accuracy, or correctness; a mistake.

Evaluation – rigorous analysis of completed or ongoing activities that determine or support the accountability, effectiveness, and efficiency of an activity or program. (http://www.businessdictionary.com/definition/evaluation.html at BusinessDictionary.com)

External assessment – the assessment process conducted by an organization outside of the CPTAC program, such as those conducted to maintain certification to a standard or certification.

Failure – In the broadest sense, a case when the system does not meet user or customer expectations; **NOTE:** This includes the inability to perform its intended functions satisfactorily or within specified performance limits. (CLSI. *Risk Management Techniques to Identify and Control Laboratory Error Sources; Approved Guideline—Second Edition.* CLSI document EP18-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2009.)

Form – a paper or electronic document on which information or results are captured; **NOTE:** Once completed, a form becomes a record.

Goal – planning element that most broadly delineates how to accomplish a specific strategy or policy at the multiprocess level.

Incorrect result – result that does not meet the requirements for its intended medical use; **NOTE 1:** In the case of quantitative test procedures, a result with a failure of measurement that exceeds a limit based on medical utility; **NOTE 2:** In the case of qualitative test procedures, a result that is contrary to a true value of the measurand.

Internal assessment – the process of gathering information on the effectiveness of the CPTAC QMS and the alignment of business and technical work processes to ensure achievement of its requirements.

Nonconformance/nonconformity/Nonconforming event – nonfulfillment of a requirement (ISO 9000 [3.6.2]).

Objective – planning element that delineates in detail how to accomplish a specific goal at the process level.

Policy – a documented statement of overall intentions and directions defined by those in the organization and endorsed by management.

Preventive action – action to eliminate the cause of a potential nonconformity or any other undesirable potential situation (ISO 9000 [3.6.4]); **NOTE 1:** There can be more than one cause for a potential nonconformity; **NOTE 2:** Preventive action is taken to prevent occurrence whereas corrective action (ISO 9000 [3.6.5]) is taken to prevent recurrence.

Procedure – specified way to carry out an activity of a process (ISO 9000 [3.4.5]).

Process – set of interrelated or interacting activities that transforms inputs into outputs (ISO 9000 [3.4.1]).

Process improvement – part of a process management focused on reducing variation and improving process effectiveness and efficiency (ISO 3534-2 [3.2.1.7]).

Product – result of a process (ISO 9000 [3.4.1]); **NOTE:** There are four generic product categories, as follows: a) services (eg, transport: a laboratory produces services such as diagnostic examinations and consultation); b) software (eg, computer program, dictionary: generally, laboratories do not produce software); c) hardware (eg, engine mechanical parts: generally, laboratories do not produce hardware); d) processed materials (eg, blood products).

Program – plan or system of actions directed at accomplishing a clear objective, with detailed activities to be taken, by whom, when and what means or resources to be utilized.

Quality – degree to which a set of inherent characteristics fulfills requirements (ISO 9000 [3.1.1]).

Quality control – part of quality management focused on fulfilling quality requirements (ISO 9000 [3.2.10]).

Quality improvement – part of quality management focused on increasing the ability to fulfill quality requirements (ISO 9000 [3.2.12])

Quality indicators – observations, statistics, or data defined by the organization or service that typify the performance of a given work process and provide evidence that the organization or service is meeting its quality intentions. (American Association of Blood Banks. *Standards for Blood Banks and Transfusion Services.* 22nd ed. Bethesda, MD: AABB; 2003.)

Quality management – coordinated activities to direct and control an organization with regard to quality (ISO 9000 [3.2.8]).

Quality management system – management system to direct and control an organization with regard to quality (ISO 9000 [3.2.3]); **NOTE:** Systematic and process-oriented efforts are essential to meet quality objectives.

Quality planning – part of quality management focused on setting quality objectives and specifying necessary operational processes and related resources to fulfill the quality objectives (ISO 9000 [3.2.9]).

Quality policy – overall intentions and direction of an organization related to quality as formally expressed by executive management (ISO 9000 [3.2.4]); **NOTE 1:** Generally the quality policy is consistent with the overall policy of the organization and provides a framework for the setting of quality objectives; **NOTE 2:** Quality management principles presented in this International Standard can form a basis for the establishment of a quality policy.

Quality system essentials – management foundation of interrelated processes that support the laboratory's path of workflow for quality management.

Record – evidence of results achieved or activities performed (ISO 9000 [3.7.6]); **NOTE 1:** Records can be used, for example, to demonstrate traceability and to provide evidence of verification, preventive action and corrective action; **NOTE 2:** Generally records need not be under revision control.

Requirement – condition or capability needed to achieve an objective that must be met or possessed by a system or system component to satisfy a standard or specification.

Review – activity undertaken to determine the suitability, adequacy, and effectiveness of the subject matter to achieve established objectives (ISO 9000 [3.8.7]).

Strategy – key element of the strategic prioritization phase of plans management that most broadly delineates how a clinical service organization can best satisfy a specific customer need; **NOTE 1:** A strategy can be time-phased as short-, medium-, or long-range and might require staging for research, development, and/or implementation; **NOTE 2:** A policy.

Supplier – organization or person that provides a product or service (ISO 9000 [3.3.6]); EXAMPLES: Producer, distributor, retailer or vendor of a product, or provider of a service or information; **NOTE 1:** A supplier can be internal or external to the organization; **NOTE 2:** In a contractual situation, a supplier is sometimes called “contractor.”

Traceability – ability to trace the history, application, or location of that which is under consideration (ISO 9000 [3.5.4]); **NOTE:** When considering a product, traceability can relate to: the origin of materials and parts; the processing history; and the distribution and location of the product after delivery.

Validation – confirmation through the provision of objective evidence that the requirements for a specific intended use or application have been fulfilled (ISO 9000 [3.8.5]); **NOTE:** Examples include validation of the process to use a new diagnostic tool, such as an automated laboratory test system or information system; or evidence-based medicine.

Verification – confirmation through the provision of objective evidence that specified requirements have been fulfilled (ISO 9000 [3.8.4]); **NOTE 1:** Examples include calibration verification of results obtained on automated testing analyzers, and patient identification; **NOTE 2:** The term “verified” is used to designate the corresponding status; **NOTE 3:** Confirmation can comprise activities such as performing alternative calculations, comparing a new design specification with a similar proven design specification, undertaking tests and demonstrations, and reviewing documents before issue.